

What is claimed is:

1. An isolated nucleic acid molecule encoding a vertebrate pheromone receptor.
2. An isolated DNA of claim 1.
- 5 3. An isolated cDNA of claim 2.
4. An isolated genomic DNA of claim 2.
5. An isolated RNA of claim 1.
6. An isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule encodes a mammalian pheromone receptor.
- 10 7. An isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a rat pheromone receptor.
8. An isolated nucleic acid molecule of claim 6, wherein the nucleic acid molecule encodes a human pheromone receptor.
- 15 9. A nucleic acid molecule of at least 12 nucleotides capable of specifically hybridizing with a unique sequence within the sequence of a nucleic acid molecule of claim 1, 2, 3, 4, 5, 6, 7, or 8.
- 20 10. A DNA molecule of claim 9.
11. An RNA molecule of claim 9.
12. A vector which comprises the isolated nucleic acid

molecule of claim 1, 2, 3, 4, 5, 6, 7 or 8.

13. An isolated nucleic acid molecule of claim 12 operatively linked to a regulatory element.

14. A plasmid of claim 12.

5 15. The plasmid of claim 14 designated VN1 (ATCC Accession No.97294).

16. The plasmid of claim 14 designated VN3 (ATCC Accession No. 97295).

10 17. The plasmid of claim 14 designated VN4 (ATCC Accession No.97296).

18. The plasmid of claim 14 designated VN5 (ATCC Accession No.97297).

19. The plasmid of claim 14 designated VN6 (ATCC Accession No.97298).

15 20. The plasmid of claim 14 designated VN7 (ATCC Accession No. 97299).

20 21. A host vector system for the production of a polypeptide having the biological activity of a vertebrate pheromone receptor which comprises the vector of claim 12 and a suitable host.

22. A host vector system of claim 21, wherein the suitable host is a bacterial cell, yeast cell, insect cell, or animal cell.

23. A method of producing a polypeptide having the

biological activity of a vertebrate pheromone receptor which comprising growing the host vector system of claim 22 under conditions permitting production of the polypeptide and recovering the polypeptide so produced.

- 5 24. A purified, vertebrate pheromone receptor.
25. A polypeptide encoded by the isolated vertebrate nucleic acid molecule of claim 1.
26. An antibody capable of specifically binding to a vertebrate pheromone receptor.
- 10 27. An antibody capable of competitively inhibiting the binding of the antibody of claim 26.
28. A monoclonal antibody of claim 26 or 27.
29. A method for identifying cDNA inserts encoding pheromone receptors comprising:
- 15 (a) generating a cDNA library which contains clones carrying cDNA inserts from an individual vomeronasal sensory neuron;
- (b) hybridizing nucleic acid molecules of the clones from the cDNA libraries generated in step (a) with probes prepared from the individual vomeronasal neuron and probes from a second individual vomeronasal neuron or from a main olfactory epithelium neuron;
- 20 (c) selecting clones which hybridized with probes from the individual vomeronasal neuron but not from the second individual vomoernasal neuron or
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the main olfactory epithelium neuron; and

(d) isolating clones which carry the hybridized inserts, thereby identifying the inserts encoding pheromone receptors.

5 30. A method of claim 29, after step (c), further comprising:

(a) amplifying the inserts from the selected clones by polymerase chain reaction;

10 (b) hybridizing the amplified inserts with probes from the individual vomeronasal neuron; and

(c) isolating the clones which carry the hybridized inserts, thereby identifying the inserts encoding the pheromone receptors.

15 31. A method of claim 29, wherein the probes are cDNA probes.

32. A method of claim 30, wherein the probes are cDNA probes.

33. The cDNA inserts identified by the method of claim 29, 30, 31 or 32.

20 34. A method for identifying DNA inserts encoding pheromone receptors comprising:

(a) generating DNA libraries which contain clones carrying inserts from a sample which contain at least one vomeronasal sensory neuron;

5 (b) contacting clones from the cDNA libraries generated in step (a) with nucleic acid molecule of claim 9, 10, or 11 in appropriate conditions permitting the hybridization of the nucleic acid molecules of the clones and the nucleic acid molecule;

(c) selecting clones which hybridized with the nucleic acid molecule; and

10 (d) isolating the clones which carry the hybridized inserts, thereby identifying the inserts encoding the pheromone receptors.

35. A method of claim 34, wherein the sample contains only one individual vomeronasal sensory neuron.

15 36. A method to identify DNA inserts encoding pheromone receptors comprising:

(a) generating DNA libraries which contain clones with inserts from a sample which contains at least one vomeronasal sensory neuron;

20 (b) contacting the clones from the DNA libraries generated in step (a) with appropriate polymerase chain reaction primers capable of specifically binding to nucleic acid molecules encoding pheromone receptors in appropriate conditions permitting the amplification of the hybridized inserts by polymerase chain reaction;

25 (c) selecting the amplified inserts; and

(d) isolating the amplified inserts, thereby

identifying the inserts encoding the pheromone receptors.

37. A method of claim 36, wherein the sample contains only one individual vomeronasal sensory neuron.

5 38. A method of claim 34, wherein the libraries are cDNA libraries.

39. A method of claim 36, wherein the libraries are cDNA libraries.

10 40. A method of claim 34, wherein the libraries are genomic DNA libraries.

41. A method of claim 36, wherein the libraries are genomic DNA libraries.

42. DNA inserts identified by the method of claim 34, 35, 36, 37, 38, 39, 40 or 41.

15 43. A method to isolate DNA molecules encoding pheromone receptors comprising:

20 (a) contacting a biological sample known to contain nucleic acids with appropriate polymerase chain reaction primers capable of specifically binding to nucleic acid molecules encoding pheromone receptors in appropriate conditions permitting the amplification of the hybridized molecules by polymerase chain reaction;

25 (b) isolating the amplified molecules, thereby identifying the DNA molecules encoding the pheromone receptors.

44. A method of claim 43, wherein the nucleic acid contained in the sample is DNA.

45. A method of claim 44, wherein the nucleic acid contained in the sample is genomic DNA.

5 46. The nucleic acid molecules isolated by method of claim 43, 44 or 45.

10 47. A method of transforming cells which comprises transfecting a host cell with a suitable vector of claim 12.

48. Transformed cells produced by the method of claim 47.

49. The transformed cells of claim 48, wherein the host cells are not usually expressing pheromone receptors.

15 50. The transformed cells of claim 48, wherein the host cells are expressing pheromone receptors.

20 51. A method of identifying a compound capable of specifically bind to a vertebrate pheromone receptor which comprises contacting a transfected cells or membrane fractions of the transfected cells of claim 48 with an appropriate amount of the compound under conditions permitting binding of the compound to such receptor, detecting the presence of any such compound specifically bound to the receptor, and thereby determining whether the compound specifically binds to
25 the receptor.

52. A method of identifying a compound capable of specifically bind to a vertebrate pheromone receptor which comprises contacting an appropriate amount of the

purified pheromone receptor of claim 24 with an appropriate amount of the compound under conditions permitting binding of the compound to such purified receptor, detecting the presence of any such compound specifically bound to the receptor, and thereby determining whether the compound specifically binds to the receptor.

53. A method of claim 52, wherein the purified receptor is embedded in a lipid bilayer.

54. A method of identifying a compound capable of activating the activity of a pheromone receptor which comprises contacting the transfected cells or membrane fractions of the transfected cells of claim 48 with the compound under conditions permitting the activation of a functional pheromone receptor response, the activation of the receptor indicating that the compound is capable of activating the activity of a pheromone receptor.

55. A method of identifying a compound capable of activating the activity of a pheromone receptor which comprises contacting a purified pheromone receptor of claim 24 with the compound under conditions permitting the activation of a functional pheromone receptor response, the activation of the receptor indicating that the compound is capable of activating the activity of a pheromone receptor.

56. A method of claim 55, wherein the purified receptor is embedded in a lipid bilayer.

57. A method of identifying a compound capable of inhibiting the activity of a pheromone receptor which

comprises contacting the transfected cells or membrane fractions of the transfected cells of claims 48 with an appropriate amount of the compound under conditions permitting the inhibition of a functional pheromone receptor response, the inhibition of the receptor response indicating that the compound is capable of inhibiting the activity of a pheromone receptor.

58. A method of identifying a compound capable of inhibiting the activity of a pheromone receptor which comprises contacting an appropriate amount of the purified pheromone receptor of claim 24 with an appropriated amount of the compound under conditions permitting the inhibition of a functional pheromone receptor response, the inhibition of the receptor response indicating that the compound is capable of activating the activity of a pheromone receptor.

59. A method of claim 58, wherein the purified receptor is embedded in a lipid bilayer.

60. The compound identified by the method of claim 51, 52, 53, 54, 55, 56, 57, 58 or 59.

61. A method of claim 51, 52, 53, 54, 55, 56, 57, 58 or 59 wherein the compound is not previously known.

62. The compound identified by the method of claim 61.

63. A pharmaceutical composition comprising an effective amount of the compound of claim 60 and a pharmaceutically acceptable carrier.

64. A method for manipulating the maternal behavior of a female subject comprising administering effective

amount of the compound of claim 60 to the female subject.

- 5 65. A method for manipulating the social behavior of a subject comprising administering effective amount of the compound of claim 60 to the subject.
66. A method for manipulating the reproductive functions of a subject comprising administering effective amount of the compound of claim 60 to the subject.
- 10 67. A method for manipulating the reproductive behavior of a subject comprising administering effective amount of the compound of claim 60 to the subject.
68. A method for increasing the fertility of a subject comprising administering effective amount of the compound of claim 60 to the subject.
- 15 69. A method for manipulating hormonal secretion of a subject comprising administering effective amount of the compound of claim 60 to the subject.
70. A method of claim 69, wherein the hormone is the luteinizing hormone release hormone.
- 20 71. A method of claim 69, wherein the hormone is the luteinizing hormone.
72. A method of claim 69, wherein the hormone is the prolactin release hormone.
- 25 73. A method of claim 69, wherein the hormone is the prolactin.

74. A method for manipulating food intake rate of a subject comprising administering effective amount of the compound of claim 60 to the subject.
- 5 75. A method of 64, 65, 66, 67, 68, 69, 70, 71, 72 or 74 wherein the subject is a human.
76. A method of 64, 65, 66, 67, 68, 69, 70, 71, 72 or 74 wherein the subject is an animal.
- 10 77. A composition for manipulating the maternal behavior of a female subject comprising effective amount of the compound of claim 60 and an acceptable carrier.
78. A composition for manipulating the social behavior of a subject comprising effective amount of the compound of claim 60 and an acceptable carrier.
- 15 79. A composition for manipulating the reproductive functions of a subject comprising effective amount of the compound of claim 60 and an acceptable carrier.
80. A composition for manipulating the reproductive behavior of a subject comprising effective amount of the compound of claim 60 and an acceptable carrier.
- 20 81. A composition for increasing the fertility of a subject comprising effective amount of the compound of claim 60.
82. A composition for manipulating hormonal secretion of a subject comprising effective amount of the compound of claim 60 and an acceptable carrier.
- 25 83. A composition of claim 81, wherein the hormone is the

luteinizing hormone release hormone.

84. A composition of claim 81, wherein the hormone is the luteinizing hormone.

5 85. A composition of claim 81, wherein the hormone is the prolactin release hormone.

86. A composition of claim 81, wherein the hormone is the prolactin.

10 87. A composition for manipulating food intake rate of a subject comprising effective amount of the compound of claim 60 and an acceptable carrier.

88. A method of 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, or 87 wherein the subject is a human.

89. A method of 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, or 87 wherein the subject is an animal.

15 90. A compound of claim 60, wherein the compound is a polypeptide.

91. A transgenic nonhuman living organism expressing DNA encoding a vertebrate pheromone receptor.

20 92. A transgenic nonhuman living organism expressing DNA encoding the polypeptide of claim 90.

93. A transgenic animal of claim 91 or 92.

94. A transgenic nonhuman living organism comprising a homologous recombination knockout of the native pheromone receptor.

95. A transgenic animal of claim 94.

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